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Carbon-13 nuclear magnetic resonance spectra of oxazoles

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The ^{13}C nmr spectra of oxazole and eight mono- and disubstituted derivatives have been analyzed with regard to the chemical shifts and the various carbon–proton coupling constants of the ring carbons. The data of the parent oxazole are compared with thiazole and 1-methylimidazole.

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On a analysé les spectres rmn du ^{13}C de l'oxazole et de huit dérivés mono ou bisubstitués du point de vue des déplacements chimiques et des différentes constantes de couplage C—H des atomes de carbone du cycle. Les données relatives à l'oxazole parente sont comparées à celles du thiazole et du méthyl-1 imidazole.

[Traduit par le journal]

In the course of our work on a new synthesis of azoles (1) we were confronted with a lack of ^{13}C nmr data of oxazoles. Thus far, only the spectrum of benzoxazole (2) and the ^1J (C, H) coupling constants of 4-methyloxazole (3) have been reported.[1] It became, therefore, worthwhile to carry out a ^{13}C nmr analysis of the oxazole ring system.

We here present the data of a series of nine oxazoles, i.e., the chemical shifts of the ring carbons (Table 1) and coupling constants (Table 3). Furthermore, these data of the parent oxazole are compared with thiazole and 1-methylimidazole (Tables 2 and 3).

Experimental

The oxazoles **4**, **6**, **7**, and **8** (Table 1) were recently prepared in our laboratory by reaction of tosylmethyl isocyanide (TosMIC) or derivatives thereof, and aromatic aldehydes (1). Samples of the oxazoles **1**, **2**, **3**, and **5** were prepared according to the literature referred to in Table 1.

The ^{13}C nmr spectra were measured in $CDCl_3$ solution at 35°C on a Varian XL 100 apparatus using the FT technique and an internal deuterium lock. The $CDCl_3$ absorptions were used as internal reference; chemical shifts were corrected to δ_{TMS} with $\delta_{TMS} = \delta_{CDCl_3} + 77.0$ ppm. Coupled spectra were recorded using the gated noise decoupling technique.

In the measurements in which the methyl protons were selectively decoupled, the low power decoupling transmitter was employed in the hetero mode. To that end the proton spectrum of the sample was recorded first (also with ^2H lock and in the CW mode) to determine the exact setting of the decoupler offset, i.e., the setting that gives a zero beat at the position of the singlet of the methyl protons.

Results and Discussion

^{13}C Chemical Shifts

Chemical shift data of the parent oxazole (**1**), three monosubstituted derivatives (**2–4**), and five disubstituted ones (**5–9**) are given in Table 1. The chemical shifts of the ring carbons have been assigned by making use of the (absence of) one-bond C—H coupling constants (^1J), and known substituent effects of aryl, methyl, methoxy, and tosyl (1*g*, 4, 5).

From this assignment the following generalizations can be made. (*1*) In all cases C(2), located between two electronegative hetero atoms, resonates at the lowest field; at ca. 150 ppm when unsubstituted, and about 10 ppm lower when substituted with methyl, methoxy, or phenyl. (*2*) The chemical shifts of C(4) and C(5), at ca. 126 and 138 ppm, respectively, when both carbons are unsubstituted, show a downfield shift of 10–15 ppm upon substitution with one aryl group and, simultaneously, an upfield shift of about 5 ppm for the other (unsubstituted) carbon.

In Table 2 the chemical shifts of the ring carbons of oxazole (**1**) are compared with thiazole **10** (5) and *N*-methylimidazole **11** (6). The highest field absorption of **1** belongs to C(4) rather than to C(5) as in **10** and **11**, which may be a reflection of the higher electronegativity of oxygen. In **10** the C(4) absorption is shifted ca. 18 ppm to lower field as compared with **1** and **11**; an almost identical difference is observed for the C(β) of thiophene with respect to furan and pyrrole (11).

Coupling Constants

All one-bond coupling constants (^1J) and most of the long range coupling constants (^2J, ^3J) of the oxazole ring atoms were easily obtained from the coupled ^{13}C spectra[2] (see Table 3). The oxazoles

[1]After this paper was submitted for publication, ^{13}C nmr spectra of a large number of benzoxazoles and oxazole were published (12). The spectral data of oxazole were almost identical to our results.

[2]The splitting patterns of the oxazole ring atoms were first order both in ^1H and ^{13}C nmr.

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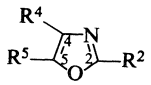
TABLE 1. ^{13}C nuclear magnetic resonance chemical shifts of the ring carbons of a series of oxazoles



Compound	Substituents			Chemical shifts[a] (ppm)			Other absorptions	Ref.
	R^2	R^4	R^5	C(2)	C(4)	C(5)		
1	H	H	H	150.6	125.4	138.1		7
2	Ph	H	H	160.9	127.6	137.7	125.4, 126.7, 127.8, 129.3	8
3	H	Tos	H	152.1	142.6	141.8	21.5, 128.2, 129.9, 136.2, 145.2	9
4	H	H	*p*-ClPh	150.1	121.3	149.8	124.9, 125.6, 128.5, 133.7	1*a*
5	Me	Ph	H	161.0	140.1	132.6	13.0, 124.7, 127.1, 128.0, 130.7	10
6	Me	H	*p*-ClPh	160.3	121.7	149.3	13.1, 124.3, 125.9, 128.2, 132.8	1*e*
7	MeO	H	*p*-ClPh	162.1	121.1	145.3	57.9, 124.1, 126.3, 128.7, 133.0	1*k*
8	H	Me	*p*-ClPh	148.5	131.0	143.8	13.2, 125.7, 126.6, 128.2, 132.8	1*j*
9	H	Benzo		152.6	140.1	150.0	110.8, 120.5, 124.4, 125.4	2

[a]Estimated errors are within ±0.3 ppm.

TABLE 2. ^{13}C nuclear magnetic resonance chemical shifts (ppm) of oxazole (**1**), thiazole (**10**), and 1-methylimidazole (**11**)

Compound	C(2)	C(4)	C(5)	CH_3
1	150.6	125.4	138.1	—
10[a]	153.6	143.3	119.6	—
11	135.8	126.7	118.3	30.7

[a]Data obtained from ref. 5.

5, **6**, **8**, and 1-methylimidazole (**11**) gave more complex signals because of additional long range coupling with the methyl hydrogens. The additional coupling could be eliminated, however, by selective irradiation of the methyl protons. For the oxazoles **5**, **6**, and **8** this decoupling did not affect the other coupling constants; only 1-methylimidazole (**11**) showed a slight reduction of the coupling constants. The ^2J and ^3J coupling constants of **11** listed in Table 3 were obtained by multiplying the measured coupling constant (J reduced) with a factor derived from the ^1J's of the selectively decoupled and the gated noise decoupled spectra of **11**, assuming a constant ratio J reduced/J for each proton.[3]

$^1J(C,H)$

In all oxazoles (**1–9**) the various ^1J's have about the same values: 230 Hz for C(2)—H(2), 194 Hz for C(4)—H(4), and 210 Hz for C(5)—H(5). This leads to the following sequence for oxazoles ^1J C(2),-H(2) > ^1J C(5),H(5) > ^1J C(4),H(4), whereas for thiazole (**10**) and 1-methylimidazole (**11**) was found ^1J C(2),H(2) > ^1J C(5),H(5) ≃ ^1J C(4),H(4). The

TABLE 3. The ^{13}C—H coupling constants (J, Hz) of the ring atoms of oxazoles **1–8**, thiazole (**10**), and 1-methylimidazole (**11**)[a]

Compound[b]	J between C(2) and			J between C(4) and			J between C(5) and		
	H(2)	H(4)	H(5)	H(2)	H(4)	H(5)	H(2)	H(4)	H(5)
1	231.1	10.7	7.9	8.9	195.3	16.5	4.1	18.9	209.1
2		[c]	[c]		193.8	16.2		18.6	207.6
3	236.2		9.0	9.3		13.7	4.0		217.2
4	230.9	11.3		8.4	194.3		4.2	17.4	
5			8.1			14.3			205.6
6		11.3			192.3			17.0	
7		12.5			193.0			15.6	
8	229.0			8.2			5.6		
10[d]	213.0	15.2	6.0	15.2	187.0	7.1	≃0	16.2	190.6
11[f]	205.9	10.6	7.0	10.7[e]	188.0	10.3[e]	3.5	16.6	188.6

[a]Estimated errors within ±0.6 Hz.
[b]For substituents of oxazoles **1–8** see Table 1.
[c]Not determined because of further coupling with the phenyl protons.
[d]Values obtained from ref. 5.
[e]Assignment might be the reverse.
[f]Values are in close analogy to data in ref. 6.

[3]See ref. 4, p. 66 ff.

greater electronegativity of oxygen causes a larger difference between the ^1J's of the oxazoles.

^{2}J (C, H)

The two-bond coupling constants of the oxazoles ^2J C(4),H(5) and ^2J C(5),H(4) have values of about 16 Hz and 18 Hz, respectively. Comparison with **10** and **11** shows that ^2J C(5),H(4) is almost independent of the nature of ring atom 1 (O, S, or N), whereas ^2J C(4),H(5) appears to increase with a larger electronegativity of atom 1 (5).

^{3}J (C, H)

In oxazoles the three-bond coupling constants are smaller than the ^2J's. The sequence in magnitude of the ^3J's for the three ring systems is for oxazole ^3J C(2),H(4) > ^3J C(4),H(2) $\simeq$ ^3J C(2),H(5) > ^3J C(5),H(2), and for thiazole and imidazole: ^3J C(2),H(4) $\simeq$ ^3J C(4),H(2) > ^3J C(2),H(5) > ^3J C(5),H(2).

The data in Table 3 show that the magnitude of the coupling constants of the oxazole nucleus is only slightly affected by substituents. This observation can be of use in structural assignments in oxazole chemistry.

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